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BY THE U.S. GENERAL ACCOUNTING OFFICE

Report To The Secretary Of Health And Human Services

FDA Should Reduce Expensive Antibiotic Testing And Charge Fees Which More Closely Reflect Cost Of Certification

The Food and Drug Administration (FDA) certifies batches of antibiotics, insulin, and color additives. Certification is the testing of batch samples for compliance with established standards and the issuing of certificates for batches that pass the tests. FDA charges fees to manufacturers to cover its cost of certification.

The current level of antibiotic testing is not necessary. The number of batches failing certification tests has historically been low. Batch certification is an expensive product assurance strategy and other less costly control mechanisms are available. Further, GAO believes FDA should revise the method for determining the fees charged manufacturers for the cost of certification.

GAO makes several recommendations to the Secretary of the Department of Health and Human Services to resolve these matters.

COMPLETED
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OCTOBER 28, 1981

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UNITED STATES GENERAL ACCOUNTING OFFICE
WASHINGTON, D.C. 20548

HUMAN RESOURCES
DIVISION

B-203267

The Honorable Richard S. Schweiker
The Secretary of Health and
Human Services

Dear Mr. Secretary:

This report discusses our review of the Food and Drug Administration's premarket testing and certification of antibiotics, insulin, and color additives. The report contains recommendations to you for reducing the level of antibiotic testing and for charging manufacturers for the cost of certification.

As you know, section 236 of the Legislative Reorganization Act of 1970 requires the head of a Federal agency to submit a written statement on actions taken on our recommendations to the Senate Committee on Governmental Affairs and the House Committee on Government Operations not later than 60 days after the date of the report and to the House and Senate Committees on Appropriations with the agency's first request for appropriations made more than 60 days after the date of the report.

We are sending copies of this report to the appropriate Senate and House Committees and Subcommittees and to the Director, Office of Management and Budget.

We would appreciate being advised of your views and any action you plan to take regarding the matters discussed in this report.

Sincerely yours,

Edward A Densmore

for Gregory J. Ahart
Director

GENERAL ACCOUNTING OFFICE
REPORT TO THE SECRETARY OF
HEALTH AND HUMAN SERVICES

FDA SHOULD REDUCE EXPENSIVE ANTIBIOTIC TESTING AND CHARGE FEES WHICH MORE CLOSELY REFLECT COST OF CERTIFICATION

D I G E S T

The Food and Drug Administration (FDA) certifies batches of antibiotics, insulin, and color additives. Certification involves the testing of batch samples for their compliance with established standards and the issuing of certificates for batches that pass the tests. Manufacturers may not market products subject to these tests until FDA certifies them. FDA charges fees to manufacturers to cover its cost of certification. The fees are deposited into a revolving fund and support 235 staff positions. The certification of antibiotics is by far the largest of the testing programs, as shown below:

	Fiscal year 1980		
Type of product	Positions supported by certification fees	Batches submitted for certification	Fees paid
			(millions)
Antibiotics	192	19,055	$5.2
Insulin	5	515	.4
Color additives	38	3,732	1.1
	235	23,302	$6.7

GAO performed this review because a comprehensive survey of FDA's monitoring of prescription drugs showed that the current level of antibiotic certification was costly and may not be necessary.

LEVEL OF ANTIBIOTIC CERTIFICATION SHOULD BE REDUCED

Although the current level of testing of insulin and color additives appears reasonable, GAO believes that FDA no longer needs to certify all batches of antibiotics. The level of antibiotic certification should be reduced because:

--The annual rate of batches rejected from certification has historically been less than 1 percent. The batches that were rejected varied over the years, but have been limited to only a few products and problems. Nearly half the batches rejected between 1970 and 1979 were not certified because of potency problems. GAO was told by two FDA officials that, except for nonsterile products, if these antibiotics had been marketed, the likelihood is slight that they would have created a life-threatening situation. (See p. 8.)

--The sample units submitted from a batch, and the testing units selected from a sample, may not necessarily represent the quality of the entire batch. (See p. 10.)

--The batch certification program is expensive. Its cost is borne by the manufacturer and, ultimately, the consumer. The most significant costs are not the certification testing fees, but inventory and warehousing costs incurred while waiting for FDA certification permitting products to be marketed. FDA had estimated in 1974 that the antibiotic industry could save between $330,000 and $480,000 for every day the certification process could be shortened. (See p. 12.)

--FDA has available other less costly means of assuring the quality of antibiotics. These efforts, especially postmarketing surveillance and inspections, should assure the continued quality of most categories of antibiotics if the level of batch certification is reduced. Some of these efforts may need to be increased. (See p. 13.)

Over the last decade, FDA has made numerous studies and proposals on changing the certification process, but has made few modifications to the process. Until recently, the number of products required to be certified has remained relatively stable changing only in response to new product introductions and marketing. However, in November 1980 the agency exempted two classes of antibiotics from certification requirements. It is now considering exempting two additional classes. However, these exemptions together account for only about 11 percent of all batches certified. (See p. 15.)

FDA's Bureau of Drugs has proposed to the Commissioner of FDA that the antibiotic certification program be changed. FDA officials told GAO that the proposal calls for (1) a gradual exemption of most classes of antibiotics from batch certification, (2) considering an increase in surveillance efforts and inspections of manufacturers' processes, and (3) a requirement for some newly approved antibiotics to be temporarily certified. (See p. 18.)

THE METHODOLOGY USED TO DETERMINE THE COSTS OF THE CERTIFICATION PROGRAM SHOULD BE REVISED

FDA uses funds derived from certification to support activities not specifically related to the certification process. The agency, therefore, uses certification fees to fund some salaries and expenses which would continue even if the certification program were reduced or eliminated. GAO believes these activities should not be considered as certification related. If FDA were to substantially reduce the level of certification, as GAO is recommending, other funds would be needed to support the non-certification-related activities now supported with certification fees.

GAO found that persons in at least 64 (about 33 percent) of the 192 positions currently supported by antibiotic fees are performing functions that appear to be unrelated to the certification process. (See p. 23.) For example:

--At least 15 of the 95 staff years in the antibiotics testing laboratory are devoted to performing unrelated activities, such as reviewing and testing manufacturers' applications to market antibiotics and testing postcertification samples.

--Five administrative positions involve such activities as reviewing manufacturers' applications to market antibiotics, authorizing antibiotic expiration periods, and drafting regulations about antibiotic products.

Tear Sheet

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--Only 2 to 5 of the 22 fee-supported district office positions may be directly related to certification. Fiscal year 1977 records showed that actual staff time spent on certification activities was practically nonexistent. There is no information to indicate that the situation has changed since that time.

FDA has also not verified the accuracy of 45 "offset" positions 1/ charged to the program, or the costs associated with those positions. The 45 positions represent equivalent staff years, not actual employees. FDA does not have an adequate method to allocate the time and costs of these positions to the certification program. (See p. 27.)

Insulin and color additive fees also support some activities unrelated to the certification of these products. (See p. 29.)

RECOMMENDATIONS TO THE SECRETARY OF HEALTH AND HUMAN SERVICES

The Secretary should require the Commissioner of FDA to

--develop a strategy for reducing the level of antibiotic testing;

--assure through selective certification and alternative means (such as inspections and post-marketing surveillance) that manufacturers continue to comply with the established standards for manufacturing antibiotics;

--periodically assess the need to continue batch certification of insulin and color additives;

--establish a more restrictive definition of "certification-related activity" to include only activities which are related directly or indirectly to the certification process;

--absorb in appropriated funds staff positions determined not to be involved in antibiotic, insulin, and color additive certification; and

--develop an accurate method for allocating staff time and cost to the certification program. (See pp. 20 and 29.)

1/Offset positions are defined on page 23.

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ABBREVIATIONS

FDA	Food and Drug Administration
GAO	General Accounting Office
HHS	Department of Health and Human Services
NCAA	National Center for Antibiotic Analysis

CHAPTER 1

INTRODUCTION

The Food and Drug Administration (FDA) as part of its efforts to assure the safety and efficacy of regulated products is responsible for certifying that manufacturers' production batches of antibiotics, insulin, and color additives are safe and, for antibiotics and insulin, effective. Certification is the testing of batch samples for their compliance with established standards and the issuing of certificates for batches that pass the tests. Manufacturers may not distribute these products until they have received a certificate from FDA. If a sample is found not to comply with standards, FDA rejects the batch and the product cannot be marketed.

The Federal Food, Drug, and Cosmetic Act of 1938, as amended (21 U.S.C. 301), requires batch certification. 1/ It directs the Secretary of the Department of Health and Human Services (HHS) to test every batch of insulin, but allows the Secretary to exempt from the requirements antibiotics and color additives that the Secretary finds do not need to be certified. The act also requires that fees be charged to manufacturers to cover the costs of certification.

About 160 manufacturers are subject to certification requirements. In fiscal year 1980, these manufacturers paid $6.7 million for FDA to certify their products, as follows:

Type of product	Number of manufacturers	Batches submitted for certification	Fees paid (millions)
Antibiotics	133	19,055	$5.2
Insulin	5	515	.4
Color additives	23	3,732	1.1
	161	23,302	$6.7

The FDA units involved in certification are in the Bureau of Drugs, Bureau of Foods, and Bureau of Veterinary Medicine. Within the Bureau of Drugs, the units primarily involved are the National Center for Antibiotics Analysis (NCAA) which tests antibiotic

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1/ The requirements for certification of (1) insulin are contained in section 506 (21 U.S.C. 356), (2) antibiotics for human use are contained in section 507 (21 U.S.C. 357), (3) antibiotics for animal use are contained in section 512(n) (21 U.S.C. 360 b(n)), and (4) color additives are contained in section 706(c)(21 U.S.C. 376(c)).

samples, the Division of Drug Biology which tests insulin samples, and the Certification Services Branch which issues both antibiotics and insulin certificates or rejection notices. Within the Bureau of Foods, the Division of Color Technology tests color additive samples and issues the certificates or notices of rejection.

HISTORY OF CERTIFICATION

The Federal Food, Drug, and Cosmetic Act of 1938 established batch certification. It required certain color additives used in foods, drugs, or cosmetics to be certified. The Color Additives Amendment of 1960 extended the requirement to all color additives. Certification of insulin began in 1941. The antibiotic certification program began following a 1945 amendment to the act subjecting penicillin to this requirement. Additional amendments in the following 8 years extended certification to new antibiotics as they were developed. The Kefauver-Harris Drug Amendments of 1962 extended the requirement for certification to all antibiotics for human use. Only five original antibiotics for animal use must be certified.

PROGRAM RESOURCES

FDA's certification programs are financed wholly by the industries affected, and fees are deposited into a revolving fund. FDA maintains separate accounting records for each program, and operating gains or losses within a program are carried forward year to year. Operating gains or losses occur when fees exceed or are less than actual operating expenses. Operating expenses for both the antibiotics and color additives programs exceeded fees collected in fiscal year 1980. These deficits were covered by prior year surpluses. The fees support salaries and other expenses of 235 authorized positions, as follows:

	Authorized positions
Antibiotics	192
Insulin	5
Color additives	38
Total	235

PRIOR GAO REVIEWS

In a September 1961 report entitled "Review of Enforcement and Certification Activities of the Food and Drug Administration, Department of Health, Education, and Welfare" (B-133350), we reported on the Department's (now HHS) programs for assuring that drugs and certain other products are safe and effective. The review included

FDA's antibiotic, insulin, and color additives certification program. We questioned the need for 100-percent premarket certification of antibiotics and proposed to the Secretary that the drug control programs be reviewed to determine whether staff and other testing resources could be better allocated. We proposed that FDA consider the relative risks of products not meeting standards and the results of past testing and control experience. Our review also disclosed that all elements of cost, particularly the cost of Government-owned space occupied by personnel performing certification services, were not included in establishing fees for those services. We proposed that FDA include the cost of space when developing data for establishing fees. FDA implemented this proposal.

In our December 1969 report entitled "Improvements Suggested in Accounting Methods Used in Establishing Fees for Reimbursable Testing and Related Services" (B-164031(2)), we reported on FDA's policies, procedures, and practices for recovering costs incurred in (1) certifying antibiotics, insulin, and color additives and (2) establishing tolerances for pesticide chemicals. Again, we found FDA was not recovering the full cost of certification. FDA was not including in its fees, salaries of administrative personnel of various groups having functions relating to certification and related support costs, such as supplies, printing, reproduction, and utilities. The review further disclosed that FDA did not use sound methods for determining employees' time spent on certification services. Some administrative costs were charged on the basis of supervisors' unsupported estimates. As discussed in chapter 3, we still question the manner in which FDA determines its costs of certification.

OBJECTIVES, SCOPE, AND METHODOLOGY

We performed this review because a comprehensive survey started in June 1980 to determine the effectiveness of FDA efforts to monitor prescription drugs indicated that the current level of antibiotic certification may not be necessary.

The objectives of this review were to examine (1) the necessity of the present antibiotics, insulin, and color additives certification programs; (2) the appropriateness of the programs' funding mechanisms; (3) the validity of positions dependent upon program revenues; (4) whether certain individual tests could be eliminated; and (5) the agency's ability to absorb the laboratory staff if the programs are reduced. We subsequently decided not to address the latter objective because we believed it should more appropriately be considered by FDA management.

FDA also certifies biologics. We did not include this program in our review because it is supported by appropriations rather than user fees, and we had recently completed a review of FDA efforts to regulate biologics (HRD-80-55, June 6, 1980).

Our review was made at FDA offices and laboratories in Rockville, Maryland, and Washington, D.C.

To assess whether the current level of antibiotics, insulin, and color additives certification is needed for each program, we looked at certification procedures, batch rejection rates, exemption policies and procedures, and alternative quality control methods. We also relied heavily on opinions of officials from FDA's Bureaus of Drugs and Foods concerning the need for certification. We concluded, based on our discussions with these officials, that the current level of insulin and color additives certification is reasonable. We, therefore, concentrated our efforts on the need to certify antibiotics.

We reviewed numerous agency reports, articles, and management studies considering alternatives to antibiotic certification; analyzed statistics on antibiotic products most often rejected and the reasons for the rejections; assessed procedures for submitting and testing batch samples; considered other quality assurance programs for antibiotics; examined certification processing time and cost burdens imposed on antibiotic manufacturers; interviewed program management officials; and reviewed the Bureau of Drugs' efforts to modify the program through exemptions and reduced testing of selected products. We also interviewed various Bureau of Drugs officials to determine what changes to the antibiotic certification program are under consideration by FDA.

We analyzed certification processing time for samples received for a 1-week period in April 1981. The Bureau of Drugs does not normally maintain the data we needed and had to specially compile it for us. We selected that week because it was current and FDA would have completed testing before completion of our fieldwork. Although the analysis may not be statistically valid, FDA certification program officials believe the certification-processing times are typical. We have no basis for concluding that the same or a different result would have occurred if a different week had been selected.

In regard to the financial aspects of this review, we examined applicable legislation and Government policies regarding user fees, reviewed certification fee cost studies and resource allocation analyses, reviewed computations of billings to manufacturers, and identified fee-supported positions and activities. With respect to billings to manufacturers, we noted several computational errors. These errors were brought to the attention of appropriate FDA officials who submitted corrected billings to the manufacturers. Our findings regarding which activities are not related to the certification process are based to a large extent on the agency's own studies and opinions. We discussed our findings with FDA program and financial management officials.

We also reviewed applicable sections of the Federal Food, Drug, and Cosmetic Act and FDA regulations. While FDA has not commented formally on this report, the report was discussed with agency officials and their comments have been incorporated in the report.

CHAPTER 2

LEVEL OF ANTIBIOTIC CERTIFICATION SHOULD BE REDUCED

FDA should reduce the current level of batch certification of antibiotics. Rejection rates for antibiotic samples submitted for testing historically have been low, sampling methods do not adequately assure that certified batches comply with established standards, alternative control measures are available, and batch certification is expensive to the manufacturer and, ultimately, the consumer.

Despite a number of FDA studies recommending changes in the antibiotic certification program, only limited changes have been made. The agency is currently considering another proposal to reduce the level of certification.

There appears to be sufficient justification for continuing the current level of certification of insulin and color additives.

THE LAW AND FDA REGULATIONS REQUIRE CERTIFICATION

As discussed in chapter 1, the Federal Food, Drug, and Cosmetic Act requires the Secretary of HHS to provide for batch certification of antibiotics, insulin, and color additives. The law provides authority to waive the requirement for certification of antibiotics and color additives, but contains no such provision for insulin.

With respect to antibiotics, section 507 of the act requires that batches be certified if they meet the standards the Secretary deems necessary to adequately insure the safety and efficacy of the product. If a batch does not meet these standards, the agency is not supposed to certify it. The law further requires the Secretary, whenever he finds certification of a drug or class of drugs is unnecessary to insure the safety and efficacy of the product, to exempt the drug from certification. The law notes that, in deciding whether to exempt a drug, the Secretary must consider whether the manufacturer (1) has produced, within 18 months, 50 consecutive batches of the drug in compliance with standards, or (2) has otherwise demonstrated consistency in production.

FDA's regulations for administering the antibiotic certification program direct its Commissioner to certify that a batch is safe and efficacious. FDA will issue a certificate if (1) the manufacturer has submitted the required information (including results of its own tests and assays) and samples, and the request

for certification contains no untrue statements, and (2) the batch complies with the regulations and conforms to applicable standards of identity, strength, quality, and purity which the regulations prescribe. The regulations further instruct the Commissioner of FDA to refuse to certify a batch if his investigation shows that information submitted or the batch covered by such request do not comply with the above requirements. The tests and methods of assay are prescribed in the regulations and are used to determine a batch's compliance with standards.

FDA NO LONGER NEEDS TO CERTIFY ALL BATCHES OF ANTIBIOTICS

The current level of batch certification of antibiotics is no longer necessary and should be reduced. FDA rejects few antibiotic batches, the agency's sampling methods do not guarantee that certified batches comply with established standards, batch certification is expensive, and other controls (such as conducting postmarketing surveillance surveys and inspecting manufacturers' facilities) are available for monitoring the quality of antibiotics. If the level of batch certification were reduced, FDA would need to reevaluate the level of its alternative monitoring strategies to assure that manufacturers continue to comply with the established standards, especially since FDA's current postmarketing surveillance efforts concentrate on antibiotics which are nearing the end of their shelf life. By gradually reducing certification, FDA can better determine how it will concentrate its efforts on other monitoring options. However, a reduced level of premarket sampling and testing should be retained as a monitoring tool particularly in the case of newly approved antibiotics or others with a history of significant or unique problems.

Some FDA officials have long questioned the need to treat antibiotics differently from other drugs. They note that, since the certification program began, other nonantibiotic drugs have been developed which match antibiotics in difficulty of manufacture and problem potential. At the same time, the technology of producing, controlling, and testing antibiotics has advanced considerably. Today, according to FDA, little or no difference is detected in the drug industry's ability to produce quality products, either antibiotics or nonantibiotics. As early as 1971, according to an FDA report, some agency officials believed that FDA should eliminate certification and assign the staff to work on other critical programs. Officials responsible for antibiotic certification agreed that the program should be modified but not eliminated.

FDA rejects few antibiotic batches

The rejection rates 1/ for antibiotic batches traditionally have been low. Since 1948, the annual rejection rate has not exceeded 1.2 percent and has been as low as 0.13 percent. Rejections which have occurred varied over the years, but have been limited to only a few products and problems. In our opinion, careful industry scrutiny may be enough to assure low defect rates, even in the absence of batch certification. FDA told us that one exception to this is the growth of foreign-produced antibiotics whose origins and manufacturing practices may be unknown.

The only exceptions to a below 1-percent rejection rate since 1948 occurred between 1962 and 1966, following legislative changes which brought many antibiotics under the certification program for the first time. The highest rejection rate during those years was 1.18 percent in 1962. The rejection rates for fiscal years 1970-80 were as follows:

Antibiotic Batches Tested and Rejected

Fiscal year	Batches tested	Batches rejected	Rejection rate (percent)
1970	(a)	126	-
1971	(a)	94	-
1972	20,898	146	0.70
1973	22,116	149	.67
1974	20,894	109	.52
1975	21,391	102	.48
1976 (note b)	25,746	105	.41
1977	20,408	103	.50
1978	20,700	81	.39
1979	21,472	50	.23
1980	19,055	30	.16

a/Not available.

b/Includes transition quarter.

1/The rejection rates are computed by dividing the number of batches denied certification by the number of batches submitted for certification.

Only a few products 1/ and problems account for most rejections. Seventy-seven percent of the 1,065 batches rejected between 1970 and 1979 were due to only 10 products and 75 percent were due to only 5 problems. These five problems were potency, sterility, moisture, penicillin contamination, and concordance (purity). Potency problems represented 46 percent of all rejections. We were informed by two FDA officials that even if the rejected batches, except those rejected for nonsterility, had gotten onto the market the likelihood is slight that they would have caused a life-threatening situation.

Rejection statistics do not consider batches that failed the manufacturers' own tests and were never submitted to FDA for certification. Nor do they consider batches manufacturers submitted before August 1976 for certification, but later withdrew because of the certainty that they would be rejected. The effect of the past practice was to understate defect rates. Since then FDA has not allowed manufacturers to withdraw samples from certification if it has begun testing and has found the samples defective. Since most manufacturers now test their batches at the same time FDA tests them, the post-1976 statistics may include batches that manufacturers found defective but were not allowed to withdraw from testing. Furthermore, the statistics do not consider batches whose rejection FDA rescinds because, for example, FDA's laboratory test results were inaccurate and the manufacturer later proved the batch was acceptable or the manufacturer modified a defective product to meet the standards. Between 1972 and 1980, FDA rescinded the rejections of an average of nearly 12 batches a year.

Low rejection rates may suggest that the industry's manufacturing and quality control procedures are adequate to preclude the need for batch certification. Alternatively, the low rates may be a result of the program; that is, because manufacturers anticipate FDA's testing, they first assure themselves that their batches are acceptable. While the certification program's effect on batch compliance rates may be speculative, FDA has attempted to predict what would happen to the rate of defective batches if batch certification were eliminated. In a 1971 survey of the program, FDA noted indications existed that the rate would rise. The survey report referred to three antibiotic products exempted in the 1950s, but which later had problems resulting in complaints of severe adverse reactions, samples which did not meet standards, and recalls.

In a 1978 evaluation of the program, FDA speculated that, although batch certification improves the quality of antibiotics

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1/A "product," as used here, is an antibiotic (or antibiotic-containing medical device) without considering its method of application. There are approximately 65 products subject to certification. Examples are tetracycline and penicillin.

which need improving, the historically low rejection rate indicates that most producers have mastered the technology. In November 1980, FDA exempted from certification all dermatological and vaginal antibiotic products (see p. 16). At the time of our review, the Bureau of Drugs had not yet collected information that would indicate the effect of this exemption on the defect rate. We believe more time is needed before a conclusion can be reached.

Sampling and testing methods may not detect all product deficiencies

Although FDA has established procedures for collecting and testing antibiotic batch samples for certification, some defective products may go undetected. The sampling regimen, as well as other factors, may limit the testing laboratory's efforts in identifying defective batches. FDA officials told us, however, that the agency has no evidence to suggest any failure to reject defective batches has occurred or that any related health problems occurred.

FDA regulations specify the size of the sample which the manufacturer must submit for certification testing and the way in which the sample is to be collected. In general, a sample is to be collected in equal intervals and is to consist of at least 1 unit for every 5,000 units in the batch. For batches over 500,000 units, however, the sample size may be up to only 100 units. It should be noted that, although FDA regulations establish the method of selecting samples, it is the manufacturer, and not FDA, which actually selects the samples to be submitted for testing. FDA also requires manufacturers to submit the results of their tests and assays made on the batch (see p. 6). The agency does not repeat all of the manufacturer's tests before certifying or rejecting the batch. The FDA testing laboratory (NCAA) chooses which ones to repeat as well as how many units in the sample to test.

The sample units submitted from a batch may not be statistically valid and may not represent the quality of the entire batch, although the guidance provided to industry seeks to assure that statistical representativeness occurs. Batch sizes may range from thousands to millions of dosage units. The trend has been to larger batches. Since sample size is not always related to batch size, a manufacturer who produces, for example, a batch of several million tablets need only submit 100 of them, the same number that would be submitted if the batch size were only 500,000 tablets.

In addition, methods of selecting sample units for testing may produce unrepresentative results. FDA selects units from a sample to test. The manner in which these units are selected and their size influence the extent to which FDA's tests will accurately characterize the batch's quality. In a 1974 study, the Bureau of Drugs found that a potential for error exists in the testing program's ability to detect defective batches. The study

found that FDA risked accepting a batch which was 10-percent defective about

--80 percent of the time when testing for potency,

--11 percent of the time when testing for sterility,

--91 percent of the time when testing for pyrogens (fever-producing substances), and

--98 percent of the time when testing for moisture.

The Bureau of Drugs attributed this risk to the small number of units being tested compared to the batch size.

A 1978 issues and options paper on the certification program prepared by the Director of the Bureau of Drugs' Office of Planning, Evaluation, and Management 1/ noted additional shortcomings in the program, including:

--The reliability of certain laboratory tests is low and no statistical statements of test variability exist. Furthermore, the laboratory has no independent unit which looks after quality assurance.

--FDA has not used manufacturers' assay results as much as possible as a check against its own test results. Little analysis of manufacturer- and FDA-generated data occurs. The agency merely makes determinations as to whether a batch passes the requirements for certification.

--The availability of resources limits the amount of testing which can take place. Consequently, the statistical confidence associated with projections of batch quality is limited.

In commenting on this, FDA officials told us that, while criticisms of the elements associated with evaluating statistical representativeness have been made in a constructive vein, no one disagrees that there is no foolproof means of establishing the absence of defects. The officials also told us that, as one answer to this issue, FDA has considered adopting a statistical extrapolation approach to judging quality rather than simply relying on the present acceptance rules. The former seeks to estimate from the test values a measure of the confidence that the batch as a whole will be of an acceptable quality.

1/This Office was formerly the Office of Planning and Evaluation and the Office of the Assistant Director for Planning and Analysis. Hereafter, it will be referred to as the Office of Planning, Evaluation, and Management.

The batch certification program is expensive

Batch certification is an expensive product assurance strategy. It has perhaps one of the highest costs per sample and demands more FDA staff time than other assurance methods. Its cost is borne by the manufacturer and, ultimately, the consumer. Manufacturers paid FDA over $5.2 million in 1980 for certification services. Moreover, manufacturers incur additional expenses associated with the certification program, primarily inventory and warehousing costs while awaiting the certification notice.

The cost of certification is continuing to rise. A new fee schedule became effective in April 1981. Of 61 individual test fees, 48 rose, 6 remained unchanged, and 7 dropped. In addition, the flat fee per batch for costs other than those related to a specific test increased 34 percent from $85 to $114. According to FDA, these increases were necessary to offset a general increase in all costs for operating the certification program.

In addition to the fees, manufacturers incur other costs in complying with certification requirements. The most significant costs are incurred while waiting for FDA certification permitting batches to be marketed. The Bureau of Drugs attempts to process 1/ most batch samples within 30 days after receiving them. We analyzed the processing time of samples received during a 1-week period in April 1981 2/ and found that FDA was generally meeting its goal. We did not attempt to assess the reasonableness of that goal. Of 405 samples received during that week, we had complete information on 388. Of these, 341 (88 percent) were processed within 30 days. Over 49 percent of these were processed in less than 21 days.

While FDA is generally meeting its processing time goal, industry's costs are substantial. The Pharmaceutical Manufacturers Association, whose membership accounted for over 70 percent of FDA's certification fee income in 1979, recently surveyed all its member firms who produce and market antibiotics. The Association found their members spent over $61.5 million on the certification program in 1979, of which $56.1 million (91 percent) was for indirect costs. Such costs consisted primarily of funds invested in inventory awaiting certification, warehousing, and lost sales. FDA has acknowledged these extra costs which the antibiotic industry

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1/Processing time is from the date FDA receives the sample to the date the certificate or notice of rejection is issued.

2/See page 4 for an explanation of the methodology we used in selecting the sample.

bears as part of the certification process. A June 1974 FDA memorandum estimated that the antibiotic industry could save between $330,000 and $480,000 for every day the certification process could be shortened. With respect to this, it should be noted that reductions in costs to the manufacturers would not necessarily be passed on to consumers.

NCAA's acting director noted that the agency may have difficulty shortening certification processing times. The number of certain tests that the laboratory can run each day depends, for one thing, on available test animals. Housing space for animals is limited and those that are housed need time to rest between tests. The length of time some equipment can be used within a given time period is also limited. Furthermore, microbiological tests are time consuming. For example, the sterility test must run a minimum of 7 days before a negative result can be reported. Another constraint is that NCAA has no control or knowledge of how many samples or what kind of samples it will receive on any given day.

Other quality controls are available to monitor antibiotics

In addition to batch certification, FDA has available a number of other product quality assurance mechanisms to determine whether marketed antibiotics meet required standards. These include conducting postmarketing surveillance surveys, inspecting manufacturers' facilities, and receiving product defect and adverse reaction reports. These programs, especially postmarketing surveillance and inspections, should assure the continued quality of most categories of antibiotics if the level of batch certification is reduced. Some FDA officials believe that, if certification were reduced, the level of some of these other efforts would need to be increased. Consequently, although reducing the level of certification may be less expensive to manufacturers, it could require additional public spending if available FDA resources are insufficient for these expanded surveillance efforts.

FDA conducts postmarketing surveys to test samples of antibiotics on the market to determine if they still meet the specifications in the regulations. The agency collects samples which are near the drug's expiration date, if they are available. The objective of this criterion is to establish that the product has remained potent and that its original chemical identity has been preserved. FDA's district offices gather the samples from manufacturers' warehouses, wholesalers, dispensing retail pharmacies, or hospitals. For fiscal year 1981, the offices are selecting one sample per product, per manufacturer, regardless of the labeled potency claim. For fiscal year 1982, FDA is proposing that offices collect samples from two batches per product, per manufacturer, for exempted products. When samples are found that

do not meet the applicable specifications, the product is recalled. For example, the fiscal year 1977 surveys led to the recall of 41 batches of antibiotics.

In addition to the sampling program, FDA is legally required to inspect all drug manufacturing facilities at least once every 2 years. While routine inspections of antibiotic manufacturers generally emphasize conformity with good manufacturing practices, occasionally special inspections will be made in conjunction with a drug application approval or when certification testing reveals a problem needing prompt attention. Manufacturers found to be in noncompliance during an inspection are required to make appropriate corrections.

FDA also uses drug defect and adverse reaction reporting systems to monitor the quality of antibiotics. These systems are intended to determine drug-induced health problems resulting from such factors as improper administration, the environment, genetic characteristics, and manufacturing defects. Both consumers and health professionals submit reports. As a result of these reports, FDA can request the manufacturer to take corrective action, seize the product, issue an injunction, or recall the product from the market.

FDA has extensively studied the certification program, but has made few changes

Despite a number of studies and proposals for changes in the certification process over the last decade, FDA has made few modifications to it. Many proposals have been made by FDA employees (at the staff level) that would alter the number of products subject to certification, the length of certification, and the amount of sample testing. FDA has been slow to adopt these changes. One of the reasons for this may be the financing problems discussed in chapter 3.

Many studies made of the certification program

Between 1971 and 1978, various groups within FDA performed at least four detailed studies of the certification program. Each study presented one or more strategies for certifying antibiotics. The four studies were:

--"Survey Report of the FDA Batch Certification Programs" (March 1971) - This survey (by FDA's Division of Management Systems, Office of Administration--now the Division of Management Systems and Policy, Office of Associate Commissioner for Management and Operations) examined a number of alternatives to FDA's certification programs

for antibiotics, insulin, and color additives. The study report did not include specific recommendations because, according to the report, such recommendations would be heavily dependent upon policy officials' decisions about acceptable degrees of product assurance.

--"Evaluation Study of the Antibiotic Certification Program" (July 1974) - This report (by the Bureau of Drugs' Office of Planning, Evaluation, and Management) described the results of a cost/benefit analysis of the antibiotic certification program. The Bureau undertook this study after the then-Acting Commissioner questioned the necessity for certifying 100 percent of the antibiotic batches. The report noted a number of alternatives the Bureau should consider if it decided to make major changes in the certification program.

--"A Strategy for Certifying Antibiotics More Effectively" (March 1976) - This paper (by the staff of the Bureau of Drugs' Office of Planning, Evaluation, and Management) suggested that the method of batch analysis be based on the particular manufacturer's competence and the risks to the consumer from individual products and tests.

--"Evaluation of the PMS [Program Management System] Project Antibiotic and Insulin Certification" (March 1978) - This report (by the staff of FDA's Associate Commissioner for Planning and Evaluation and the Bureau of Drugs' Office of Planning, Evaluation, and Management) concentrated on antibiotic certification. The staff recommended requiring batch approval as a condition for marketing antibiotics, but lifting this requirement unless it is believed that a drug will not meet manufacturing standards and may pose health risks.

At the time of our review, FDA's Bureau of Drugs was drafting another proposal for changing the certification program. (See p. 18.)

FDA has taken little action to change certification procedures

FDA has not exempted many products subject to certification nor changed significantly the amount of sample testing. Until recently, the number of products required to be certified has remained relatively stable changing only in response to new product introductions and marketing. However, in November 1980, the agency exempted two classes of antibiotics and has cut back on the frequency and type of testing of selected products.

The Federal Food, Drug, and Cosmetic Act gives FDA the flexibility to exempt antibiotics from the certification requirements. (See p. 6.) A 1975 HHS' Office of the General Counsel memorandum noted that the law allows for eliminating or modifying all antibiotic certification by regulation, without changing the statute.

Before November 1980, the FDA regulations which carried out the law's exemption provision authorized the exemption only of antibiotics for local or topical use, and then only under the following conditions:

--The antibiotic had to have been marketed commercially as a drug for 5 years and in the particular dosage form for 2 years.

--The manufacturer had to submit a petition to the Commissioner of FDA establishing that within 18 months the petitioner had produced and had submitted for certification not less than 50 consecutive batches of the drug, or not less than 25 consecutive batches of the drug and not less than 25 consecutive batches of other associated antibiotic drugs of the same dosage form, none of which had failed to meet the standards.

--The petitioner had to have done all laboratory tests and assays required as a condition for certification. Also, the petitioner could not distribute a batch of the drug until such tests and assays found the drug in compliance with the certification specifications.

The regulations stipulated that the exemption was only applicable to the petitioner requesting it. FDA was to publish notice of any granted exemptions in the Federal Register.

Manufacturers rarely sought to use the exemption provision. In July 1979, FDA reported that within the previous 2 years the agency had received only five petitions involving six dermatological drug products. The agency granted two of the petitions for three of the products. The remaining products were later exempted under a November 1980 blanket exemption for dermatologicals and vaginals.

The only other exemptions we could find that occurred before November 1980 were in the early 1950s. However, FDA revoked these exemptions in 1972 when some batches were found not to meet FDA standards.

In the November 28, 1980, exemption, FDA amended its regulations to include a blanket exemption for all dermatologic and vaginal antibiotics. The Federal Register announcement of the

amendment called the exemption a first step toward a program to change or eliminate batch certification requirements which are no longer needed to insure antibiotic drugs' safety and efficacy. FDA's tentative conclusion was that the advanced state of manufacturing technology and manufacturers' high level of compliance with existing requirements generally warrants exempting certain classes of antibiotics from batch certification. FDA exempted dermatologic and vaginal products first because limited provisions for their exemption already existed. Also, FDA considered their method of application as posing less risk to the public than other forms. As a result of this exemption, 108 drugs produced by 28 manufacturers are no longer subject to batch certification.

During our review the Bureau of Drugs was drafting a proposal to exempt otic and ophthalmic (ear and eye) antibiotic drugs from required batch certification. The proposal noted that these products have shown a consistently high level of quality in their manufacture. In addition, their method of use is similar to that for dermatologic and vaginal products.

Despite these actions to reduce the number of products subject to certification, the impact is limited. The dermatologic/vaginal and otic/ophthalmic exemptions account for only about 11 percent of all batches certified.

In addition, FDA has made only limited efforts to reduce sample testing. HHS' Office of the General Counsel stated that the law indicates FDA does not have to test batches before certifying them. FDA may rely on the results of tests and assays which manufacturers requesting certification submit. These results, however, usually give one value for each test or assay or merely indicate satisfactory compliance. A single reported value may be the result of one test, or an average of a number of tests. Also, FDA believes it cannot determine from a single value how many tests the manufacturer did or whether the manufacturer did the tests properly. Therefore, results submitted by manufacturers are of limited value in FDA's concluding how much testing it should do or, ultimately, if the batch meets FDA requirements. For this reason, FDA proposed in 1977 that manufacturers submit all results of their own testing, including the mean value of each test and any test results which did not meet the specified standards. The agency could then decide on the level and type of testing needed.

FDA never put the 1977 proposal into effect. It was withdrawn 3 years later because the benefits of requiring the additional data did not justify the additional burden to manufacturers and FDA. According to comments FDA received, the possibility of FDA's doing fewer duplicative tests did not justify the added cost of submitting the additional test data or the certification delays caused by FDA's analyzing the data.

In May 1979 and again in December 1980, the Chief of the Certification Services Branch suggested that the 1977 proposal go into effect on a voluntary basis only for selected product classes. He suggested that the manufacturers of those products be asked to submit more detailed data on their test results. FDA, in turn, would do selective testing. The Branch Chief noted that FDA would then receive much better assurances for the batches it does test and minimal assurance for all batches and that certification time should decrease. The Bureau of Drugs' management, however, did not adopt the Branch Chief's recommendation apparently because of a proposal being considered for major changes in the program.

NCAA has recently reduced or eliminated some testing on selected products. It made these cuts based on such factors as (1) the producer's past performance, (2) subsequent testing that will be performed on a product in its final form, and (3) the existence of more than one test that provides the same information. Under unusual demand circumstances, FDA has also foregone certain testing activities, depending instead on a review of manufacturer data.

THE BUREAU OF DRUGS PROPOSES TO REVISE THE CERTIFICATION PROGRAM

In May 1981, during our review, the Director of the Bureau of Drugs 1/ approved a draft proposal to change the antibiotic certification program. The proposal was presented to the Commissioner of FDA at a July 1981 briefing. As of September 15, 1981, the proposal was awaiting the Commissioner's approval. Bureau of Drugs officials told us that the proposal's essential points include:

--Over the next 2 to 3 years most categories of antibiotics would be exempted from the certification requirement. The order of exemptions would generally reflect their relative health risks as well as the availability and suitability of alternative quality assurance strategies. Some products might be exempted on an individual manufacturer basis. Others might have their exemptions delayed.

--The active ingredients manufactured in bulk form is the only category of antibiotics not scheduled for exemption. This category would continue to be certified to monitor the quality of the bulk products manufactured by the many foreign producers of bulks, which have been of uncertain

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1/The proposal was also approved by the Director of the Bureau of Veterinary Medicine. Some antibiotics for animal use are currently subject to certification requirements.

quality, and to eliminate problems other manufacturers who use the bulk products may have with poor quality bulk.

--As certification of antibiotics is discontinued, the Bureau of Drugs would consider increasing its postmarketing surveillance efforts and inspections of antibiotic manufacturers' processes. The proposal apparently does not provide details on how much these efforts would be increased, or any additional resources needed to carry them out.

--Temporary certification may be required of newly approved antibiotics which pose high health risks and on which a manufacturing performance record has not been established.

CERTIFICATION OF INSULIN AND COLOR ADDITIVES MAY STILL BE JUSTIFIED

The continued certification of insulin and color additives may be justified. Based on information obtained from officials closely associated with these programs, the current level of certification appears reasonable. According to these officials, certification of insulin is necessary because of the drug's critical nature and production technology. Insulin is a lifesaving drug injected daily by over a million diabetics. As a biological drug, its production is more difficult to control. Variations may be detrimental to users. Furthermore, the Chief of the Certification Services Branch believes that certification should continue because insulin production is changing and expanding with the entrance of new firms on the market and the advent of new production techniques.

Officials involved in the color additives program noted that the agency decides to either require or exempt from certification an additive at the time the manufacturer requests permission to market the product. The decision is based on a review of the product, considering such factors as the likelihood that manufacturers can produce the additive according to specifications and the toxicological and safety concerns if manufacturers do not meet specifications. The officials we interviewed believed that generally the products subject to certification should not be exempted. In addition, manufacturers can petition to have FDA discontinue batch certification of a product. However, a Bureau of Foods official said no manufacturer has ever submitted a petition requesting such an exemption.

CONCLUSIONS

While the reasons given for continuing the current level of certification of insulin and color additives are reasonable, we believe that the current level of premarket certification of antibiotics could be reduced. Although a number of studies and

proposals have been made over several years to change the antibiotics certification program, only limited reductions have been made in the certification program. We believe that changes have been slow primarily because of the personnel and financing problems discussed in the following chapter of this report.

We believe that a phased reduction (but not elimination) of the program is desirable. The selective testing and certification of products plus the use of other product quality assurance mechanisms should provide reasonable assurance that safe and effective products are being marketed. At the same time, FDA can retain the capability to test products that may not meet standards.

Despite our conclusion that the current level of certification of insulin and color additives may be justified, we believe FDA should periodically review the requirements for such certification to determine whether it continues to be necessary.

RECOMMENDATIONS TO THE SECRETARY OF HHS

We recommend that the Secretary require the Commissioner of FDA to

- --develop a strategy for reducing the level of antibiotic testing,
- --assure through selective certification and alternative means (such as inspections and postmarketing surveillance) that manufacturers continue to comply with the established standards for manufacturing antibiotics, and
- --periodically assess the need to continue batch certification of insulin and color additives.

CHAPTER 3

THE METHODOLOGY USED TO DETERMINE THE COSTS OF THE CERTIFICATION PROGRAM SHOULD BE REVISED

FDA uses funds derived from the certification program (fees charged to manufacturers) to support activities not specifically related to the certification process. Therefore, FDA uses certification fees to fund some salaries and expenses which would continue even if there were no certification program. Also, it is not using substantiated methods to allocate some costs to the certification program. If FDA were to substantially reduce the level of certification, as we are recommending in chapter 2, other funds would be needed to support the non-certification-related activities now supported by certification fees.

LAWS AND GOVERNMENT POLICIES REQUIRE CERTIFICATION FEES

Laws, regulations, and an Office of Management and Budget circular provide instructions for charging manufacturers for certification services. The Federal Food, Drug, and Cosmetic Act requires the Secretary of HHS to promulgate regulations prescribing fees as necessary to provide, equip, and maintain an adequate certification service for antibiotics, insulin, and color additives. Antibiotic regulations require manufacturers to pay a flat fee for each batch of antibiotic drugs they submit plus individual fees for each test done during the certification process. The regulations list the individual fees. Regulations governing insulin and color additives also specify fees manufacturers must pay to have their products certified.

The Independent Offices Appropriation Act of 1951 (31 U.S.C. 483a) and the Office of Management and Budget Circular A-25 provide further guidance for charging fees. Title V of the act requires that any work, service, or certificate furnished to a person be self-sustaining to the fullest extent possible. The act also authorizes agency heads to prescribe fees which they determine to be fair and equitable, considering direct and indirect costs to the Government, value to the recipient, the public policy or interest served, and other pertinent factors. Circular A-25 states that the Federal Government should impose a reasonable charge on each identifiable recipient to recover the full cost to the Government of a service providing a special benefit. The charges must cover direct and indirect costs to the Government of carrying out the activity including (1) salaries, retirement, and employee insurance; (2) depreciation of buildings and equipment; (3) rent and maintenance of buildings and equipment; (4) a proportionate share of the agency's management and supervision; and (5) enforcement, research, and establishment of standards to the extent that the

agency head determines that these costs are properly chargeable to the activity. The Circular directs that the cost of providing a service be reviewed each year and fees adjusted as necessary.

FDA's Division of Financial Management conducts cost studies to determine appropriate fees for antibiotics, insulin, and color additives certification. The most recent of these studies for antibiotics, dated January 1981, revises the fee schedule which had been in effect since 1976. The most recent fee study for insulin was in May 1980 and the most recent fee study for color additives was in May 1977. A revised color additives fee study is currently being finalized.

SOME FEES SUPPORT ACTIVITIES NOT RELATED TO CERTIFICATION

Fees received under FDA's antibiotic certification program are supporting activities not related to certification. FDA uses certification fees to fund some salaries and expenses which do not have a direct or indirect relationship to the certification process. If certification were phased out, FDA would need other funds to continue these unrelated activities.

Although the Federal Food, Drug, and Cosmetic Act authorizes FDA to charge for certification services, it does not define what activities are necessary to "provide, equip, and maintain an adequate certification service." In our opinion, a certification-related activity is one which would not continue if FDA were to phase out certification. Under our approach certification-related activities should include only laboratory testing of antibiotic batch samples, certificate issuance, certification-related research, and managerial/administrative support related to these activities. If FDA reduces certification, the agency will also reduce its need for these activities.

FDA, however, has a different interpretation of what qualifies as a certification-related activity. One official in the Bureau of Drugs stated that the Bureau defines certification activities as those needed to "regulate" antibiotics. Regulation of antibiotics would include approval of new antibiotics for marketing, postmarketing surveillance, and inspecting drug firms. Agency studies and other documents describe antibiotic certification as consisting of reviewing drug applications, developing standards, testing batch samples, developing new test methods, monitoring marketed products, and other activities. Although the Office of Management and Budget Circular A-25 suggests that these kinds of activities should be considered in determining fees, we do not believe that, in this case, such activities should be charged to the certification program. Except for batch testing, many antibiotic-related activities would continue even without a certification program.

The antibiotic certification fees support 192 positions within FDA. These positions are distributed as follows:

Distribution of Fee-Supported Positions

Organizational unit	Number of positions
Bureau of Drugs:	
NCAA testing branches	95
NCAA, Office of Director	6
NCAA, Sample Control staff	6
Laboratories Services staff	23
Certification Services Branch	12
Certifiable Drug Review staff	5
Other Bureau of Drugs	13
Bureau of Veterinary Medicine	2
Office of the Commissioner, including Associate Commissioner for Management and Operations	8
Executive Director of Regional Operations	22
Total	192

FDA's Division of Financial Management projects that salaries and related personnel expenses of these 192 positions will account for almost 75 percent of the program's total projected budget for fiscal year 1982. Remaining costs will be for such items as operating expenses (supplies, travel and transportation, printing, and service contract costs), laboratory equipment, and space rental. Space rental is allocated to the program based on the square feet of space used by direct and indirect labor for certification activities.

In its cost studies, the Division of Financial Management classifies certification-funded personnel costs into three groups: direct labor, indirect labor, and "offset" labor. Offset labor includes FDA's overhead costs charged to the program. It is supposed to represent the cumulative time spent on certification-related activities by all FDA employees, excluding the direct and indirect labor. The method for determining costs associated with these positions is discussed on page 27. Using our more restrictive approach to what constitutes a certification-related activity, we analyzed the activities of each personnel group to find out if they performed certification-related activities. We found that persons in at least 64 (about one-third) of the currently fee-supported positions are performing functions we believe to be unrelated to the certification process. To the extent that positions charged to the certification program are overstated, non-personnel costs are also overstated. The following sections discuss our findings in greater detail.

Direct labor

Our examination of FDA's direct labor shows a large proportion of this work does not meet our definition of certification-related activities. We estimate that at least 15 of the 95 staff years charged to the certification program are devoted to activities other than antibiotic certification. This does not include time spent on administrative matters by the direct labor staff or any portion of research performed which is not directly related to antibiotic certification. The amount of such unrelated research may be substantial.

FDA's direct labor consists of the personnel in NCAA's laboratory branches. Of 99 positions within these branches, FDA funds 95 with certification fees. FDA's appropriation supports the other four positions. The Division of Financial Management projects direct labor costs to total $2,657,231 for fiscal year 1982, excluding costs for the four appropriation-funded positions.

In an October 1980 study of NCAA activities, the Acting Director found that only 48 of NCAA's 99 laboratory staff years directly involve certification. The 99 staff years were allocated as follows:

Allocation of NCAA staff

Activity	Staff years
Certification	48
Research	25
Reviews and tests of antibiotic drug applications	11
Administration	10
Tests on postcertification samples	5
Total	99

An undetermined amount of the administrative time is related to certification. In addition, consistent with our definition, research activities should be considered certification-related activities only when they are directly related to certification testing.

Various Bureau of Drugs officials agreed that NCAA is performing other than certification activities. These officials consider unrelated functions to include postmarketing surveillance and other postcertification sample testing; pyrogen testing (testing fever-producing substances) of nonantibiotics, new drug application reviews and testing, development of standards, research (as discussed below), contaminants research, and residue analysis. The

Associate Director for Pharmaceutical Research and Testing maintains that many of NCAA's laboratory activities, such as those listed, should continue even without a certification program. He believes that laboratory expertise is needed to monitor drug quality whether regulation is through certification or through some other process.

Although we did not quantify the amount of research that would continue in the absence of certification, a 1978 study by the Bureau of Drugs' Office of Planning, Evaluation, and Management estimated that 13.5 positions in fiscal year 1978 were involved in non-certification-research activities. Most research done at NCAA is to develop new or different methods of testing antibiotics. FDA's Associate Commissioner for Management and Operations believes this type of research would continue even without certification, although less may be done. The Associate Director for Pharmaceutical Research and Testing agreed that developing methods of testing antibiotics should continue because NCAA would still do postmarket testing of antibiotics.

For fiscal year 1981, we found that NCAA planned several projects involving 3.5 staff years that were not directly related to developing methods of testing antibiotics. The NCAA management agreed these activities were not certification activities. However, the Associate Director for Pharmaceutical Research and Testing believes such projects are necessary to maintain expertise equal to that of the pharmaceutical industry.

In memorandums discussing NCAA research, the Associate Director for Pharmaceutical Research and Testing stated that much research simultaneously supports drug application reviews, postmarketing surveillance, and residue testing, as well as certification. He said no sharp break exists in the laboratory technology separating the needs of these various regulatory programs. He noted that, even without certification, a need exists for research on antibiotics to improve and guide their regulation.

Indirect labor

Some of FDA's indirect labor is also not certification related. According to our definition, at least 15 of the 52 indirect labor positions charged to antibiotic certification should not be. As with direct labor, many jobs and activities now certification funded would continue if certification is reduced.

Indirect labor costs are for staff in the Certification Services Branch, the Certifiable Drug Review staff, the NCAA Director's Office and Sample Control staff, and the Laboratory Services staff. This group consists of 52 fee-supported positions. The Division of Financial Management projects the cost for salaries and related personnel expenses for this group to be $1,241,053 for fiscal year 1982.

The Certification Services Branch has 12 positions supported by antibiotic certification fees. Its activities include reviewing and comparing NCAA and manufacturers' test results and issuing certificates for batches of antibiotics and insulin, directing the antibiotic and insulin compliance programs in pre- and postmarketing sampling and inspection, and issuing certificates for batches of three nonantibiotic drugs.

Although antibiotic certification fees support these activities, some are neither related generally to regulating antibiotics nor specifically to certifying them. For example, antibiotic certification fees support the certification (at no cost to their manufacturer) of three nonantibiotic drugs--digoxin, digitoxin, and prednisone. One staff member devotes about 25 percent of his time to these drugs. Antibiotic certification fees also pay for the Certification Services Branch's labor costs associated with regulating insulin. 1/ This activity requires about 25 percent of a staff year. Some of the Certification Services Branch's other fee-supported activities do concern regulating antibiotics, but they are not specifically related to certification. These activities include directing the compliance programs for postmarket sampling and facilities' inspections. The Branch Chief estimated that considering all its activities, the Branch would continue to need 7 of its 12 positions even if the antibiotic certification program did not exist.

The Certifiable Drug Review staff represents another group of indirect labor costs. Antibiotic certification fees pay for five of this staff's positions. The staff's principal activities are

--reviewing manufacturers' applications to market antibiotics for which standards already exist;

--approving amendments to all previously approved applications to market antibiotics;

--reviewing stability data and authorizing antibiotic expiration periods; and

--recommending, reviewing, and drafting regulations about antibiotic products for human use.

1/Although the Division of Financial Management allocated a percentage of the Branch's total labor costs to the insulin budget, it did not subtract a corresponding percentage from the antibiotic budget when it determined the antibiotic test fees. Thus, both the antibiotic and insulin budgets are charged with the labor costs associated with insulin activities, about $5,900.

A 1978 Bureau of Drugs' Office of Planning, Evaluation, and Management study found none of the Certifiable Drug Review staff's functions dependent on certification activities. This staff's functions would remain essentially the same regardless of the existence of a certification program.

Indirect labor also includes three groups (NCAA's Office of the Director, Sample Control staff, and the Laboratory Services staff) which assist NCAA direct labor in its laboratory branches. To the extent that these groups assist NCAA direct labor in activities not related to certification, they, too, are performing noncertification functions. For example, the NCAA Acting Director noted that one of six clerks on the Sample Control staff is involved in monitoring the distribution and flow of postcertification samples. In addition, 2.7 of the 23 Laboratory Support staff positions allocated to the antibiotics program are also allocated to the insulin program. Only the insulin program should support these positions.

Offset labor

The number of "offset" labor positions actually involved in certification of antibiotics is questionable. Of the 45 positions now charged to the program, only about one-fourth of them can be firmly tied to certification work.

The offset labor positions, together with a proportionate share of nonsalary and nonspace costs, appear to be the method adopted by FDA to recoup its overhead costs for administering the program. The 45 offset positions charged to the antibiotic certification program are located in the Bureaus of Drugs and Veterinary Medicine, the Office of the Commissioner, and the Executive Director of Regional Operations. Offset labor activities include accounting, program planning and evaluation, financial and personnel management, and postmarket sample collection. The Division of Financial Management projects these offset labor costs will total $1,313,412 for fiscal year 1982.

Unlike the direct and indirect labor, the 45 offset positions are supposed to represent equivalent staff years supporting certification work, not actual employees. We were unable to determine, and FDA officials were unable to explain, how the number of offset positions was originally established. The number was apparently established many years ago. In recent years, the Division of Financial Management has included the 45 offset positions in its fee studies without determining whether the number is accurate.

To determine the labor expenses of each position, the Division in its 1981 fee study used the cost of a GS-11/step 4, which is considered to be the average grade of the staff most associated with certification activity. The Division has not attempted to

verify whether the average grade level used in computing the cost of the offset positions is correct. The Division also added $4,500 to the cost for each position, which represented an estimate of the average amount needed to equip and maintain that position. The $4,500 included such expenses as travel and supplies.

In 1978, the Bureau of Drugs' Office of Planning, Evaluation, and Management studied the distribution and use of FDA's fee-supported positions to determine how each position related to certification activities. One of the study's major findings was that most of the offset activities are not uniquely related to certification and, therefore appropriations, rather than certification fee income, could fund them. The study found that:

--Of the 13 Bureau of Drugs positions allocated to antibiotic certification, financial management functions involving less than one position a year are unique to the certification program.

--Both of the offset positions in the Bureau of Veterinary Medicine are certification related.

--Of the eight positions in the Office of the Commissioner, about half are exclusively related to certification.

--Only 2 to 5 of the 22 district office positions may be directly related to certification. A review of the staffing records for fiscal year 1977 showed that actual staff expenditures on certification activities were practically nonexistent. There is no information to indicate that the situation has changed since that time.

Although the study proposed converting positions not related to certification to appropriations, the Director of the Bureau of Drugs, in consultation with the Division of Financial Management, delayed such action because of a poor budget climate. The conversion has not yet been made.

FDA does not have a method to allocate overhead positions to the certification program. Staff do not submit time records nor are periodic reviews performed to use as a basis for allocating these positions. In a December 1969 report entitled "Improvements Suggested in Accounting Methods Used in Establishing Fees for Reimbursable Testing and Related Services" (B-164031(2)), we found that the salary costs of persons performing certification program services, but not working solely on one program, were allocated based on inadequate verification of their time. We suggested that continuous time reporting, statistical sampling of time on various activities, work-measurement studies, or other cost-finding techniques could be appropriate in determining employees' time and related costs.

INSULIN AND COLOR ADDITIVE FEES ALSO SUPPORT NONCERTIFICATION ACTIVITIES

Insulin and color additive fees also support some activities unrelated to the certification of these products. As with antibiotics, we believe that these costs have been included in the fees for insulin and color additive certification primarily because of FDA's broad interpretation of certification-related activities. Until FDA revises its definition of certification-related activity, manufacturers will be charged for these costs.

For example, we found that:

--The insulin fees include a share of indirect labor costs attributable to a Bureau of Drugs unit that does no work on the insulin certification program.

--Insulin fees also support a proportionate share of the Certification Services Branch's noncertification activities.

--The color additives fees include the cost of reviewing manufacturers' petitions to market color additives and conducting routine facilities inspections. However, one appropriated position exists to cover non-certification-related activities.

CONCLUSIONS

FDA broadly defines "certification-related activity" to include activities which, in our view, should not be included. Thus, we believe that FDA should more restrictively define the cost of providing certification services and establish an accurate method for allocating expenses to the program. To do this, FDA would need to determine, such as in the case of antibiotic certification activities, which employee positions are not related to certification, but currently charged to certification, and transfer those positions to appropriated funds. To the extent that appropriated funds are not available to absorb these positions, additional funds would need to be requested. These positions should be financed through appropriated funds since employees in these positions are performing noncertification activities.

RECOMMENDATIONS TO THE SECRETARY OF HHS

We recommend that the Secretary require the Commissioner of FDA to:

--Establish a more restrictive definition of "certification-related activity" to include only activities which are related directly or indirectly to the certification process.

--Absorb in appropriated funds staff positions determined not to be involved in antibiotic, insulin, and color additive certification.

--Develop an accurate method for allocating staff time and cost to the certification program.

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